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MINERAL IMBALANCE, ENDOCRINES AND HAIR TISSUE MINERAL ANALYSIS

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The recognition of the importance of trace elements in health and disease has been gradually increasing, and has now become much more appreciated. For instance, in the past, many genetic diseases have been found to be related to mineral imbalances, such as, acrodermatitis enteropathica, a genetic disorder, which is caused by a deficiency of zinc. Menkes's disease, an inherited inborn metabolic error is associated with copper deficiency. Wilson's disease, another inborn error of metabolism is related to copper toxicity. Selenium deficiency is related to Keshan disease. More recently however, studies have found mineral imbalances related to many common health problems, such as chromium and diabetes, magnesium, zinc, copper and heart disease, zinc and iron, and immune disorders, to mention a few.

Based on this current research, it should be understood that the determination of nutritional deficiencies and excesses are important, however, the relationship, or balance between the nutrients is more important. This was emphasized by Vitale and associate in the following statement, "From a global stand-point, although dietary deficiency is definitely at the more serious end of the spectrum, the opposite end, dietary excesses and aberrations, may contribute to the burden of disease."⁽¹⁾ This was further reiterated, "Nutrition no longer deals with fully reversible single deficiencies but with imbalances, and faulty regulation of metabolic events, which may or may not have a dietary etiology."⁽²⁾ It is now recognized that nutritional imbalances can lead to subclinical deficiencies that are estimated to outnumber frank deficiencies by ten to one.⁽²⁾

Balance between nutrients is particularly important among the micro and macro elements. As stated by Davis, "trace elements have to some degree an interrelationship with other major nutrients such as proteins, carbohydrates, lipids, macro elements, and vitamins."⁽³⁾

Through our own research, and research by other investigators, we have found that hair tissue mineral analysis (HTMA) is an excellent method of assessing mineral relationships.

Materials and Methods

The development of tissue mineral analysis of human hair has helped considerably in understanding the complex relationship among minerals. The analysis of hair mineral concentrations has been available for over two decades. A conservative estimate of the number of tests performed during this time easily exceeds one million. Routine use of HTMA by physicians throughout the United States and abroad has led to significant clinical findings

that can be applicable in many specialties. The relationship between mineral deficiencies, excesses, and toxic metal exposures to health conditions have frequently been identified in patients through the use of HTMA after other methods have failed. The value of HTMA is further increased with the understanding of mineral relationships and their affects upon health and disease. These relationships are readily depicted in HTMA patterns, that otherwise would go undetected. Hair is an easily obtained biopsy material. Within this biopsy material is contained the minerals incorporated during its development,⁽⁴⁾ providing a record of long term nutritional intake.⁽⁵⁾ Multiple minerals can be tested and these mineral interrelationships can then be revealed.

Preferably, hair samples should be taken from several areas of the scalp that include; the region from the top or vertex of the head above the ears, to the nape of the neck. Samples obtained from several locations within this area of the scalp will give a more representative view than samples taken from just one area.⁽⁶⁾ The hair strands should be cut at the scalp and should be no longer than one and one-half inches in length. If the patient's hair is several inches long, only the proximal portion of the sample should be submitted for analysis. Any hair preparation such as shampoos, conditioners, and dyes used by the patient should be noted on the test request form when the sample is submitted to the laboratory.

The ideal, or mean mineral levels and ratios found in the hair are shown in Table 1. For additional clarity, the mean's of the levels are discussed here, instead of ranges and standard deviations.

It should be emphasized that this data is based upon results obtained according to this laboratory's technique that is reviewed and approved by the federal clinical laboratory-licensing agency. All levels are reported in milligrams percent (mg%).

Mineral Interrelationships

As expected, a multitude of mineral interrelationships can be complex. For example, a single mineral in the body, either too much or too little, can have an influence upon at least two other minerals, which in turn affect two more, etc. The most recognized relationships among minerals are their antagonisms. Antagonisms can occur at the intestinal level, such as when a mineral with a higher atomic weight competes with minerals of a lower atomic weight for absorption. This is well known in the case of heavy metals, such as lead, cadmium, and mercury, which compete with most of the nutritional elements. However, nutritional elements can adversely affect one another just as readily. For example, calcium directly affects the absorption of iron, zinc, phosphorus, and magnesium.⁽¹²⁾ These antagonistic effects can also occur within the tissues where an excessive accumulation of a mineral can cause compartmental displacement and the eventual excretion of another element. On the other hand, deficiencies of elements can also result in excessive accumulation of other elements (13).

This delicately orchestrated relationship demonstrates the importance of evaluating minerals in accordance to their ratios. Excessive calcium intake for example can lead to a disturbance in the Ca/P, Ca/Mg, Ca/Fe, Zn/Cu, and Fe/Cu ratios. An elevated calcium and magnesium level, even if both are above normal would indicate increased magnesium requirements if the Ca/Mg ratio is elevated. Conversely, an individual who develops a magnesium deficiency would then have decreased calcium requirements. The co-factors, or synergists, would also be increased, or decreased accordingly.

Minerals also work in cooperation or synergistically. As an example, even though iron and copper are mutually antagonistic, a proper concentration of copper is required for iron to be utilized.^(13,14) Even though calcium, magnesium, and phosphorus are mutually antagonistic, together in the proper balance, they contribute to the integrity and maintenance of osseous structures.

Vitamin-Mineral Interrelationships

Minerals also affect vitamins, and vice versa, both antagonistically and synergistically. Some vitamin deficiencies can adversely affect the absorption and/or utilization of a mineral. Rickets, a disorder of calcium metabolism is associated with a deficiency of vitamin D. A lack of vitamin C, B2, and vitamin A is associated with iron deficiency.⁽¹⁵⁻¹⁷⁾ Vitamin A itself cannot be mobilized from the liver without adequate amounts of zinc.⁽¹⁸⁾ Excessive intake of a single vitamin can also lead to a disturbance in mineral balance. For example, vitamin C is antagonistic to copper and with excessive intake may induce copper deficiency.⁽¹⁹⁾ Similarly, it may lead to excessive iron accumulation.⁽²⁰⁾ Excessive vitamin C may therefore lead to a disturbance in the Fe/Cu, and Zn/Cu ratios. By the same token, excessive copper intake may result in deficiency of vitamin C, or increase its requirement.⁽²¹⁾ Excessive intake of vitamin D, by enhancing calcium absorption, can contribute to a deficiency of magnesium and potassium,⁽²²⁾ thereby adversely affecting the Ca/Mg, Ca/P, Ca/K, and Na/K ratios. High intake of vitamin A can increase calcium excretion,⁽²³⁾ and affect the above ratios in the opposite direction.

Factors Influencing Tissue Mineral Profiles

The value of HTMA is not in establishing a diagnosis of an absolute mineral deficiency only, but in evaluating relative deficiencies and imbalances. When looking at HTMA profiles, one should be aware of the factors that influence these mineral patterns. One of the major factors is the neuro-endocrine system. Hormones affect nutritional status, especially the minerals, at several levels; absorption, excretion, transport, storage, and metabolic utilization. It can be said that diet is what is consumed, but nutrition is what is retained and utilized by the body. The neuro-endocrine system plays a major role in one's nutritional status. This is why one diet, even if all the required nutrients are present, will not satisfy everyone's nutritional needs. The presence of adequate nutrients in the diet does not insure retention or utilization of those nutrients. A limited review of some of the endocrine-mineral relationships is discussed below.

Parathyroid

Parathyroid hormone (PTH), calcitonin and vitamin D are the major hormones regulating calcium and phosphorus. They influence calcium through their effect upon intestinal absorption, bone resorption and renal reabsorption. The renal reabsorption of phosphorus, sodium and potassium is decreased by increased PTH levels.⁽²⁵⁾ PTH exerts a greater influence on calcium than magnesium and therefore can produce a relative magnesium deficiency, or increase its requirements.⁽²⁶⁾ Adequate PTH is required for the conversion of vitamin D to its active form. Plasma vitamin D3 metabolites are usually elevated during hyperparathyroid states,⁽²⁷⁾ and have similar activity to PTH.

HTMA indications of increased PTH activity include an elevated Ca/P ratio (greater than 3.0), with an elevated Ca/Mg ratio (greater than 13), and a Ca/K ratio greater than 4.2.⁽²⁸⁾

Decreased PTH indications include a decreased Ca/P ratio (less than 2.63), decreased Ca/Mg (less than 7), and lastly, a low Ca/K ratio (less than 4).

Pancreas

The release of insulin from the pancreas is calcium dependent. Calcium also stimulates insulin release.⁽²⁹⁾ Insulin can in turn stimulate parathyroid activity, since insulin enhances the activity of vitamin D, and vitamin D enhances the synthesis of insulin.^(30,31) Insulin has a similar control of the same minerals affected by PTH, and therefore increases calcium retention.⁽³²⁾ Insulin also enhances chromium excretion.^(33,34)

HTMA indications of increased insulin levels, are a Ca/P ratio greater than 3.0 and Ca/Mg greater than 14.⁽³⁵⁾ Decreased insulin indicators include; Ca/Mg less than 3, Ca/K less than 4, and the Na/K ratio less than 2.

Ovarian

Estrogen has an influence on copper,^(36,37) and zinc status.⁽³⁸⁾ Estrogen can affect the same minerals affected by insulin and PTH, in that it decreases calcium excretion.⁽³⁹⁾ Studies have shown a relationship between elevated estrogen and insulin during pregnancy and estrogen therapy.⁽⁴⁰⁻⁴³⁾ PTH secretion is actually enhanced by estrogen.^(44,45)

Progesterone has a similar effect as adrenal cortical hormones,⁽⁴⁶⁾ and is closely related to the mineral zinc.⁽⁴⁷⁾

HTMA indications of elevated estrogen include, Zn/Cu ratio less than 8, Ca/Mg greater than 8, Ca/K greater than 4, and the Ca/P ratio greater than 2.63.

Indications of decreased estrogen include, Zn/Cu greater than 8 and Ca/K less than 4.⁽⁴⁸⁾

Adrenal

Increased epinephrine levels produce cellular potassium retention,^(49,50) mediated by Na-K ATPase.⁽⁵¹⁾ This in turn can result in increased aldosterone production, which enhances sodium retention, in order to compensate for the increased potassium retention. Increased aldosterone and glucocorticoids promote calcium and magnesium losses from the body.^(52,53) Corticosteroids also interfere with vitamin D metabolism and therefore decreases calcium retention.⁽⁵⁴⁾ Copper deficiency is frequently noted with increased adrenal activity,⁽⁵⁵⁾ while decreased adrenal activity increases copper and magnesium retention.⁽⁵⁷⁻⁵⁹⁾

Increased *anabolic* adrenal cortical activity as indicated on HTMA profiles includes, Na/K greater than 5, Na/Mg greater than 4 and Ca/Mg greater than 10. Decreased activity includes, Na/Mg less than 4 and the Ca/K ratio less than 4.2.

Increased adrenal *catabolic* dominance is indicated by a decreased Na/K ratio less than 1.8, Ca/K less than 4, Ca/P less than 2.63, Ca/Mg less than 8, and the Ca/Na ratio less than 1.75.

Thyroid

Elevated thyroid activity increases calcium excretion,⁽⁶⁰⁻⁶²⁾ and abnormally affects the calcium to potassium ratio. Thyroid hormones also promote magnesium losses.⁽⁶³⁾ Thyroxine has effects which parallel those of adrenal glucocorticoids in that they can reciprocally stimulate each other,^(64,65) and therefore affect many of the same mineral ratios as the adrenal glands.

Increased thyroid activity is indicated by HTMA ratios of Ca/K less than 4, Ca/P less than 2.63, and an elevated Na/Mg ratio greater than 4. Also, the Fe/Cu ratio would be greater than 2.

Lowered thyroid activity is indicated by a Ca/K ratio greater than 4, Ca/P ratio greater than 2.63, Na/Mg ratio less than 4, Fe/Cu ratio less than 1.1, and the Zn/Cu ratio greater than 8.

As exemplified with the mineral relationships, one should be aware of the synergistic and antagonistic relationships between the endocrine glands.



The thyroid and parathyroid hormones appear to oppose each other. Frequently, hypothyroid patients show elevated PTH levels in the presence of normal serum calcium.^(66,67) Hyperthyroidism apparently decreases the activity of vitamin D and PTH.⁽⁶⁸⁻⁷¹⁾ Calcitonin antagonizes the effects of PTH.⁽⁷²⁾ Adrenal steroids, particularly glucocorticoids also antagonize PTH,^(73,74) and insulin competes with thyroxine.⁽⁷⁵⁾ Effects of the endocrine glands upon mineral retention and excretion are shown in Table 2.⁽¹¹⁾

The endocrine glands will therefore affect the mineral relationships or ratios. These are shown in Table 3.

Heavy Metal Levels and Ratios

Heavy metals can be readily assessed through HTMA. Any metal found above the lower limit should be considered as potentially toxic. Toxic ratios also should be given special consideration. The lower limits of the heavy metals routinely tested, as well as the toxic ratios are shown in Table 4. The toxic ratios are determined by comparing the heavy metal to the nutrient mineral known to antagonize that metal. For example the Ca/Pb ratio compares an individual's lead level to their calcium level. This ratio should be at least 84:1. In other words, calcium should be at least 84 times higher than lead. A ratio below 84:1 would indicate a potential toxicity of lead, even if the lead is within an acceptable level. This is illustrated in a study of autistic children.⁽⁷⁶⁾ HTMA was performed on a group of children suffering from autism, and a control group. The report concluded that lead was not a significant factor in the autistic group compared to the controls. This is understandable since the lead results were 0.62 mg% for the autistic group and 0.6 for the control group. This is not statistically significant in itself, however, after examining the data more closely, the toxic ratios revealed that lead may be a significant factor. The Ca/Pb ratio in the autistic group averaged 38:1 (well below the ideal of 84:1), while the control group was 158:1. This definitely reveals a very significant difference between the two groups.⁽⁷⁷⁾

In conclusion, not only do the endocrines affect mineral levels and ratios, but minerals in turn can have a powerful influence upon the endocrine system.

Assessing the mineral ratios through HTMA profiles, offers a unique insight into the world of metabolic and endocrine activity. HTMA offers an easily obtained and unique window to internal metabolic events that otherwise are at best extremely difficult to obtain. HTMA can be one of the most useful laboratory tests for evaluating nutritional status and requirements, especially minerals, when evaluated according to their physiological ranges and interrelationships. With continuing research and incorporation of tissue mineral tests as a routine part of the patient exam, further substantiation and usefulness of HTMA will be realized. Thereby, improving its reliability and understanding as a primary screening tool for nutritional, metabolic, and endocrine assessment.

<u>ELEMENT</u>	<u>IDEAL</u>
Calcium	42
Magnesium	6
Sodium	24
Potassium	10
Copper	2.5

Zinc	20
Phosphorus	16
Iron	2.8
Manganese	0.15
Chromium	0.08
Nickel	0.20
Selenium	0.08

<u>RATIOS</u>	<u>IDEAL</u>
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Calcium/Phosphorus	2.63
Calcium/Potassium	4.20
Calcium/Magnesium	7.10
Calcium/Iron	15.0
Calcium/Sodium	1.75
Sodium/Potassium	2.4
Sodium/Magnesium	4.0
Zinc/Copper	8.0
Iron/Copper	1.12

Table 1

<u>ENDOCRINE</u>	<u>INCREASED RETENTION</u>	<u>INCREASED EXCRETION</u>
Adrenal Cortex (Anabolic)	Na, K, P, Fe, Mn	Ca, Mg, Cu
Adrenal Cortex (Catabolic)	Na, K, P, Fe, Mn	Ca, Mg, Cu, Cr
Thyroid	P, Na, K, Fe, Mn	Ca, Mg, Cu
Parathyroid	Ca, Cu	P, Mg, Cr, Na, K, Fe, Mn
Pancreas (Endocrine)	Ca, Cu	P, Mg, Fe, Na, Zn, K, Cr
Estrogen	Cu, Ca	Zn, P, Mg, Na, K, Fe, Mn, Cr
Progesterone	Zn, Mg, Na, K, P, Fe	Ca, Cu

Table 2

ENDOCRINE	RATIOS INCREASED	RATIOS DECREASED
Parathyroid	Ca/P, Ca/Mg, Ca/Na Ca/K, Ca/Fe	Fe/Cu
Thyroid	Na/Mg, Fe/Cu	Ca/P, Ca/K
Adrenal Cortex (Anabolic)	Na/K, Na/Mg, Fe/Cu Ca/Mg	Ca/P, Ca/K, Ca/Na
Adrenal Cortex (Catabolic)	Fe/Cu, Na/Mg	Na/K, Ca/K, Ca/P, Ca/Mg Ca/Na,
Pancreas	Ca/P, Ca/Mg, Ca/K Ca/Fe, Ca/Na	Zn/Cu, Fe/Cu
Estrogen	Ca/Mg, Ca/P, Ca/K Ca/Na, Ca/Fe, Na/K	Zn/Cu, Fe/Cu
Progesterone	Zn/Cu, Fe/Cu	Na/K, Ca/K

Table 3

ELEMENT	UPPER LIMIT (Mg%)
Mercury	< 0.10
Cadmium	< 0.04
Lead	< 0.5
Aluminum	< 1.0

TOXIC RATIOS	LOWER LIMIT
Calcium/Lead	> 84:1
Iron/Lead	> 5.6:1
Iron/Mercury	> 28:1
Zinc/Cadmium	> 500:1
Zinc/Mercury	> 200:1

Table 4